Oxycodone Conditioned Place Preference and Aversion in Mice

Lauren Bystrom, Emilia Lefevre[1], & Patrick Rothwell[1,2]

Departments of [1]Neuroscience and [2]Medicine, University of Minnesota

Abstract

Opiate-based analgesic drugs, such as morphine and oxycodone, are regularly prescribed for the treatment of chronic pain. However, these drugs are extremely addictive and their overuse has led to an opioid abuse epidemic in the United States. Today, there has been a lot of research done on the mechanisms of morphine in the brain and how it may promote changes in the brain chemistry that lead to addiction. As a newer drug, Oxycodone hasn't been studied nearly as much, however in clinical practice, it is being prescribed more often. In this study, our approach was to measure both the positive reinforcing properties of oxycodone and the aversion to naloxone precipitated withdrawal using a conditioned place preference (CPP) and aversion (CPA) test, respectively.

Methods

Conditioned Place Preference
- 16 C57/B6 mice (8 male, 8 female)
- Alternating environments
  - Oxycodone and Saline Paired
  - Injections
- Baseline and Test→ no injection
  - Both environments present
- Preference Test

Conditioned Place Aversion
- 31 C57/B6 mice (16 male, 15 female)
- Alzet Pumps with Saline or Oxycodone
- Drug paired side
  - Naloxone or Saline Injection
- Baseline and Tests→ no injection
  - Both environments present
  - Test 1 with pump, Test 2 without
- Aversion Test

Results

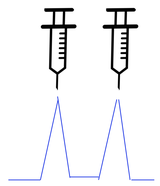
- CPP showed a 9.4% increase
  - Reinforcing Properties
- The CPA showed a 13.1% decrease
  - Withdrawal's motivational aversion

Future Directions

This research is critical because we do not currently have a good understanding of how Oxycodone's rewarding and reinforcing properties can develop into abuse and addition. With this model that we have established our lab will then be able to study the biological mechanisms underlying Oxycodone withdrawal.

Conditioned Place Preference

Injection introduces Oxycodone→ results in spike

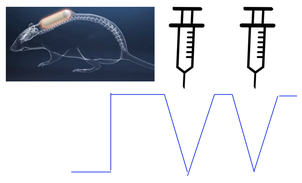


Preference Test → If drug side preferred, more time spent there on test

Conditioned Place Aversion

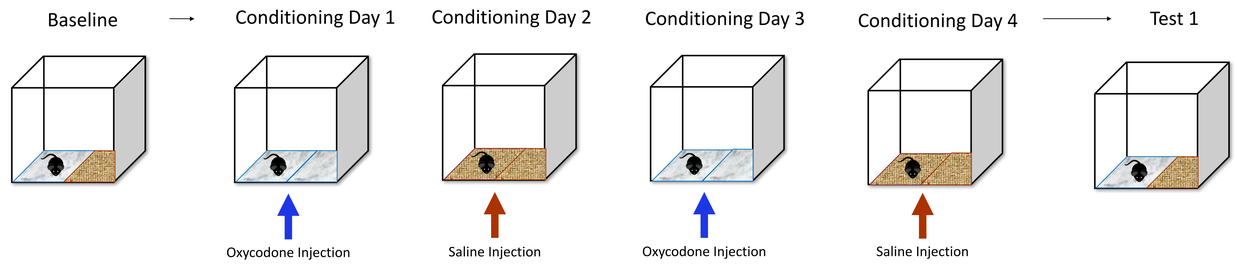
Pump introduces drug→ higher baseline

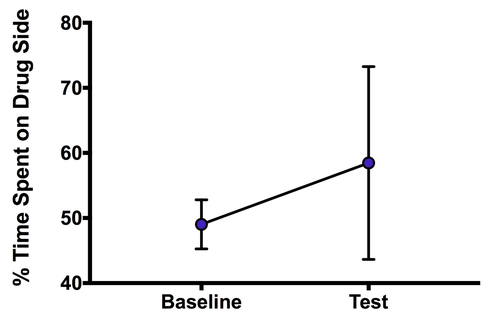
Injection introduces Naloxone→ antagonist of opioid receptor→ results in dip

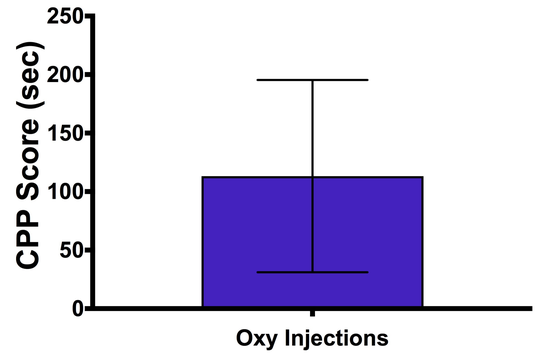


Aversion Test → If drug side aversive, less time spent there on test

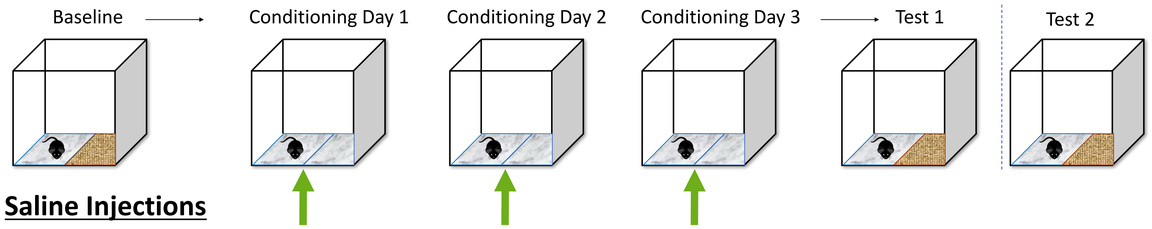
Conditioned Place Preference



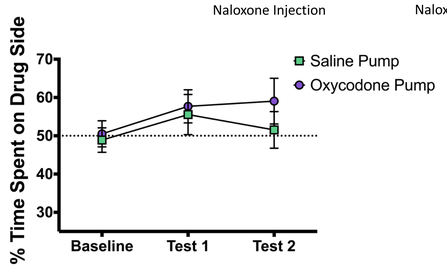


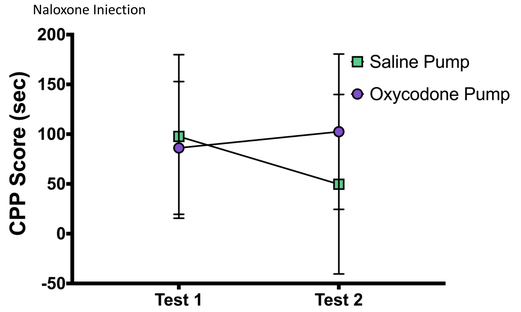


Conditioned Place Aversion

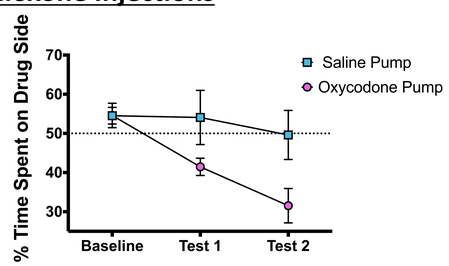


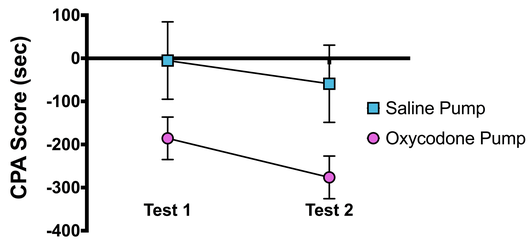
Saline Injections





Naloxone Injections





Conclusions

Conditioned Place Preference

More time spent on Oxycodone paired side

↓

Oxycodone is rewarding and reinforcing

↓

Go back to this state

Conditioned Place Aversion

Less time spent on Naloxone paired side

↓

Oxycodone withdrawal is an aversive experience

↓

Avoid this state

Take more Oxycodone

We acknowledge the rest of the Rothwell Lab. This study was funded by the University of Minnesota's Undergraduate Research Opportunity as well as MnDrive Brain Conditions and grant R00 DA037279.